

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 07-1008-WO-US)

In the Application of:)	
)	
Alastair David G. Lawson et al.)	
)	Examiner: Joanne Hama
Serial No.: 10/578,384)	
)	Group Art Unit: 1632
Filing Date: January 16, 2007)	
)	Confirmation No. 1913
For: Methods for the Treatment of)	
Inflammatory Bowel Disease)	

**DECLARATION OF ALASTAIR DAVID G. LAWSON, DIANE MARSHALL
AND TIMOTHY BOURNE UNDER 37 C.F.R. § 1.131**

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

I, Alastair David G. Lawson and I Timothy Bourne and I Diane Marshall, in support of the above-identified United States patent application, do declare and state as follows:

1. We are the first, original, and joint inventors of the subject matter claimed in United States Patent Application Serial No. 10/578,384, filed on January 16, 2007, and entitled "Methods for the Treatment of Inflammatory Bowel Disease," which claims priority benefit of International Application PCT/GB04/04652 filed November 3, 2004, which claims the benefit of Great Britain application 0325836.5 filed November 5, 2003. We submit this Declaration to overcome the Section 102(e) rejection of this patent application based on United States Patent Publication US 2005/0059113 to Bedian et al. (hereinafter "Bedian"), which was filed on September 9, 2004 and claims priority to U.S. Provisional Patent Application No. 60/502,163, filed on September 10, 2003 (the priority

date of Bedian). The Bedian application issued September 22, 2009 as U.S. Patent No. 7,592,430.

2. We, at all relevant times herein, were and remain employees of Celltech R&D Limited, of 208 Bath Road, Slough, Berkshire, SL1 3WE, United Kingdom, predecessor-in-interest of the current assignee of this application, UCB Pharma S.A., 60 Allee de la Recherche, Brussels, Belgium.

3. We conceived the inventions disclosed in the above-reference patent application well prior to September 10, 2003 (the priority date of Bedian). We also exercised diligence in reducing our inventions to practice from at least prior to September 10, 2003, with both actual construction to practice as set forth in Exhibit 1 appended hereto, and continuing through to the constructive reduction to practice evidenced by filing the original Great Britain patent application on November 5, 2003.

4. Accompanying this Declaration is Exhibit 1, which evidences our efforts to diligently reduce the inventions to practice prior to that September 10, 2003.

5. Exhibit 1 is a copy of selected pages of laboratory notebook No. 10015850 (maintained by Dr. Diane Marshall). The pages of the notebook included in Exhibit 1 are the cover, Accession page, the Table of Contents page (partially redacted), and pages 1-30 and 53-67. These are the pages in the notebook relating to the use of anti-CSF-1 antibody as a treatment for DSS-induced colitis in mice. The dates on the pages of the notebook in this Exhibit have been redacted. Each original page of the notebook included two dates, one in the upper right-hand corner and one in the lower right-hand corner. The date in the upper right-hand corner represented the date that the experiment was conducted. The date in the lower right-hand corner represented the date that the various graphs and data sheets were physically affixed in the notebook. The upper-right hand corner dates of said pages are all dated prior to September 10, 2003. The lower right-hand corner dates of pages 1-30 and 53-59 are all dated prior to September 10, 2003.

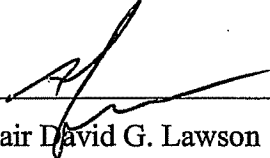
6. The currently amended claims of the present application relate to a method for the treatment of inflammatory bowel disease (IBD) comprising administering a therapeutically effective amount of an inhibitor of CSF-1 activity to a patient in need thereof, wherein said inhibitor of CSF-1 activity is selected from one or more of an anti-CSF-1 antibody, or a CSF-1-binding fragment of an anti-CSF-1 antibody. This subject matter is reflected in the work recorded in Exhibit 1. At page 1, it is reported that anti-CSF-1 antibody significantly reduced disease severity of DSS-induced colitis in mice, as noted by reduced loss of body weight, less colonic shortening, reduced colonic disease symptoms (diarrhea, blood, profuse bleeding) reduced clinical disease scores (colonic disease and weight loss), reduced number of CD3⁺ cells and neutrophils in the colon. Graphs in the Exhibit illustrating this work correspond to the figures of the present patent application. Thus, application Fig. 1 corresponds to the top figure on page 2 of Exhibit 1; application Fig. 2 corresponds to the bottom figure on page 2 of Exhibit 1; application Fig. 3a corresponds to the top figure on page 3 of Exhibit 1; application Fig. 3b corresponds to the bottom figure on page 3 of Exhibit 1; application Fig. 4a corresponds to the top figure on page 4 of Exhibit 1; application Fig. 4b corresponds to the bottom figure on page 4 of Exhibit 1; application Fig. 5 corresponds to the figure on page 22 of Exhibit 1; and application Fig. 6 corresponds to the bottom figure on page 26 of Exhibit 1. Each of these pages in the original is dated in the upper right-hand corner with a date prior to the September 10, 2003 priority date of the Bedian reference.

7. All of the work referred to in this declaration occurred in the United Kingdom, except the filing of the present application which occurred in the United States through our patent counsel, Woodcock Washburn.

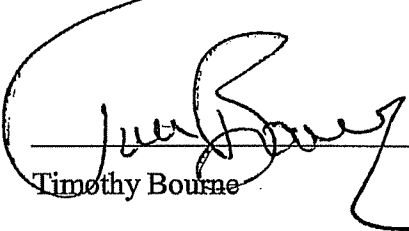
8. We hereby acknowledge that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under

Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

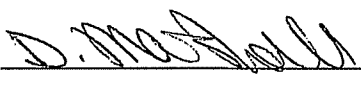
Date: 9th October 2009


Alastair David G. Lawson

Date: 9th October 2009


Timothy Bourne

Date: 9/10/09
9th October 2009


Diane Marshall

NAME:

PROJECT No:

NOTEBOOK ACCESSION No: 10015850

DATE STARTED:

DATE COMPLETED:

REDACTED

ACCESSION PAGE

1. This Notebook and all data recorded therein are the property of CELLTECH R & D LIMITED. All contents are strictly confidential. The Notebook must be returned to the company upon completion, upon request, or upon termination of employment.
2. The persons to whom this Notebook is assigned must take every precaution to safeguard against loss. In the case of fire, theft, or disappearance of this Notebook, the employee must immediately notify their Head of Department. A written report describing the circumstances of the loss must follow.
3. All persons using the Notebook and their line manager must give a specimen signature in the relevant section below.
4. Full details on how to complete the Notebook are available in the relevant procedure: 'R & D Notebook Record Keeping (Non-GLP Studies)' procedure (for Non-GLP) SOP No. GLP-SOP-MAN-16 (for GLP).

PROJECT TITLE: GENEX 130

GLP STUDY: YES() NO() X NOTEBOOK NO: 10015850

ASSIGNED TO: D. NAKSANA DATE OF ISSUE: _____
(SCIENTIST NAME(S))

CONTINUED FROM NOTEBOOK NO: _____ DATE: _____

CONTINUED TO NOTEBOOK NO: _____ DATE: _____

INSPECTED BY: _____ DATE: _____
(Line Management)

TO BE COMPLETED BY ALL NOTEBOOK SIGNATORIES.

NAME (PRINTED)	SIGNATURE	INITIALS	DATE
----------------	-----------	----------	------

REDACTED

DATE	TABLE OF CONTENTS	PAGE No.
	Effect of d-CSF-1 on DSS colitis in mice	1-30
	Report of d-CSF-1 on DSS colitis in mice	53-59
	Report 3 of d-CSF-1 on DSS colitis in mice	60-67

DATE

TABLE OF CONTENTS

PAGE No.

TITLE: Anti-CSF-1 in DSS-induced colitis in mice

PAGE No. 1

DATE

PROJECT NO

NOTEBOOK NO

10015 856

- DSS model of IBD (mice)

Aim

To assess the effects of anti-CSF-1 antibody on DSS induced colitis in mice.

Procedure

Licence: 70/5748, procedure 19.

B6/c mice (males, batch RM5305, arrived 18-24g) weighed and injected subcutaneously with mAb @ 10mg/kg.

Group 1 - 101.4, control antibody (lot: 10014426/15) - (Y1 isotype)

Group 2 - Anti-CSF-1, alkylated Ab33 (4.7mg/kg)

10 mice in each group. Normal drinking water then replaced with 1% DSS (CN MW 36-50K, Cat No 160110) in tap water 24 hours after 1st antibody injection. 4x 4-5g 9F

Group 3 - No treatment control group

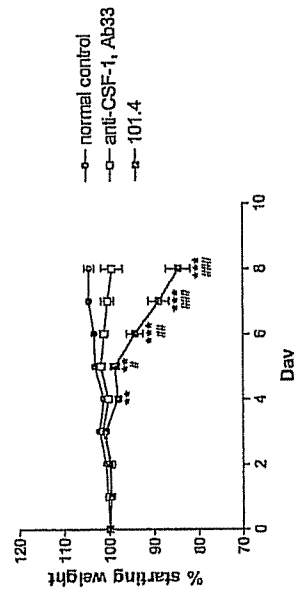
10 mice will continue to have normal drinking water.

Mice will receive antibody once a week. Animals will be weighed each day and signs of disease (loose stools, bleeding) noted. The volume of 1% DSS or water consumed also measured by weight. At end of expt., colons will be removed and length measured. A 1 cm section will be collected from the distal end for assessment of neutrophil and T cell infiltration by FACS analysis. The next 2 cm section will be collected and placed in formalin for histological analysis. The next cm will be placed in culture medium for 24 hours, after which time the supernatant will be collected and cytokine levels measured by luminex. Plasma will also be collected at termination.

Study Period

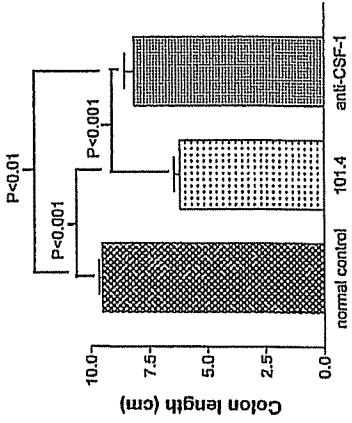
11/08/2001
10/09/2001
11/09/2001
12/09/2001
1/10/2001
2/10/2001
3/10/2001
4/10/2001
5/10/2001
6/10/2001
7/10/2001
8/10/2001
9/10/2001
10/10/2001
11/10/2001
12/10/2001
1/11/2001
2/11/2001
3/11/2001
4/11/2001
5/11/2001
6/11/2001
7/11/2001
8/11/2001
9/11/2001
10/11/2001
11/11/2001
12/11/2001
1/12/2001
2/12/2001
3/12/2001
4/12/2001
5/12/2001
6/12/2001
7/12/2001
8/12/2001
9/12/2001
10/12/2001
11/12/2001
12/12/2001
1/1/2002
2/1/2002
3/1/2002
4/1/2002
5/1/2002
6/1/2002
7/1/2002
8/1/2002
9/1/2002
10/1/2002
11/1/2002
12/1/2002
1/2/2003
2/2/2003
3/2/2003
4/2/2003
5/2/2003
6/2/2003
7/2/2003
8/2/2003
9/2/2003
10/2/2003
11/2/2003
12/2/2003
1/3/2004
2/3/2004
3/3/2004
4/3/2004
5/3/2004
6/3/2004
7/3/2004
8/3/2004
9/3/2004
10/3/2004
11/3/2004
12/3/2004
1/4/2005
2/4/2005
3/4/2005
4/4/2005
5/4/2005
6/4/2005
7/4/2005
8/4/2005
9/4/2005
10/4/2005
11/4/2005
12/4/2005
1/5/2006
2/5/2006
3/5/2006
4/5/2006
5/5/2006
6/5/2006
7/5/2006
8/5/2006
9/5/2006
10/5/2006
11/5/2006
12/5/2006
1/6/2007
2/6/2007
3/6/2007
4/6/2007
5/6/2007
6/6/2007
7/6/2007
8/6/2007
9/6/2007
10/6/2007
11/6/2007
12/6/2007
1/7/2008
2/7/2008
3/7/2008
4/7/2008
5/7/2008
6/7/2008
7/7/2008
8/7/2008
9/7/2008
10/7/2008
11/7/2008
12/7/2008
1/8/2009
2/8/2009
3/8/2009
4/8/2009
5/8/2009
6/8/2009
7/8/2009
8/8/2009
9/8/2009
10/8/2009
11/8/2009
12/8/2009
1/9/2010
2/9/2010
3/9/2010
4/9/2010
5/9/2010
6/9/2010
7/9/2010
8/9/2010
9/9/2010
10/9/2010
11/9/2010
12/9/2010
1/10/2011
2/10/2011
3/10/2011
4/10/2011
5/10/2011
6/10/2011
7/10/2011
8/10/2011
9/10/2011
10/10/2011
11/10/2011
12/10/2011
1/11/2012
2/11/2012
3/11/2012
4/11/2012
5/11/2012
6/11/2012
7/11/2012
8/11/2012
9/11/2012
10/11/2012
11/11/2012
12/11/2012
1/12/2013
2/12/2013
3/12/2013
4/12/2013
5/12/2013
6/12/2013
7/12/2013
8/12/2013
9/12/2013
10/12/2013
11/12/2013
12/12/2013
1/1/2014
2/1/2014
3/1/2014
4/1/2014
5/1/2014
6/1/2014
7/1/2014
8/1/2014
9/1/2014
10/1/2014
11/1/2014
12/1/2014
1/2/2015
2/2/2015
3/2/2015
4/2/2015
5/2/2015
6/2/2015
7/2/2015
8/2/2015
9/2/2015
10/2/2015
11/2/2015
12/2/2015
1/3/2016
2/3/2016
3/3/2016
4/3/2016
5/3/2016
6/3/2016
7/3/2016
8/3/2016
9/3/2016
10/3/2016
11/3/2016
12/3/2016
1/4/2017
2/4/2017
3/4/2017
4/4/2017
5/4/2017
6/4/2017
7/4/2017
8/4/2017
9/4/2017
10/4/2017
11/4/2017
12/4/2017
1/5/2018
2/5/2018
3/5/2018
4/5/2018
5/5/2018
6/5/2018
7/5/2018
8/5/2018
9/5/2018
10/5/2018
11/5/2018
12/5/2018
1/6/2019
2/6/2019
3/6/2019
4/6/2019
5/6/2019
6/6/2019
7/6/2019
8/6/2019
9/6/2019
10/6/2019
11/6/2019
12/6/2019
1/7/2020
2/7/2020
3/7/2020
4/7/2020
5/7/2020
6/7/2020
7/7/2020
8/7/2020
9/7/2020
10/7/2020
11/7/2020
12/7/2020
1/8/2021
2/8/2021
3/8/2021
4/8/2021
5/8/2021
6/8/2021
7/8/2021
8/8/2021
9/8/2021
10/8/2021
11/8/2021
12/8/2021
1/9/2022
2/9/2022
3/9/2022
4/9/2022
5/9/2022
6/9/2022
7/9/2022
8/9/2022
9/9/2022
10/9/2022
11/9/2022
12/9/2022
1/10/2023
2/10/2023
3/10/2023
4/10/2023
5/10/2023
6/10/2023
7/10/2023
8/10/2023
9/10/2023
10/10/2023
11/10/2023
12/10/2023
1/11/2024
2/11/2024
3/11/2024
4/11/2024
5/11/2024
6/11/2024
7/11/2024
8/11/2024
9/11/2024
10/11/2024
11/11/2024
12/11/2024
1/12/2025
2/12/2025
3/12/2025
4/12/2025
5/12/2025
6/12/2025
7/12/2025
8/12/2025
9/12/2025
10/12/2025
11/12/2025
12/12/2025
1/1/2026
2/1/2026
3/1/2026
4/1/2026
5/1/2026
6/1/2026
7/1/2026
8/1/2026
9/1/2026
10/1/2026
11/1/2026
12/1/2026
1/2/2027
2/2/2027
3/2/2027
4/2/2027
5/2/2027
6/2/2027
7/2/2027
8/2/2027
9/2/2027
10/2/2027
11/2/2027
12/2/2027
1/3/2028
2/3/2028
3/3/2028
4/3/2028
5/3/2028
6/3/2028
7/3/2028
8/3/2028
9/3/2028
10/3/2028
11/3/2028
12/3/2028
1/4/2029
2/4/2029
3/4/2029
4/4/2029
5/4/2029
6/4/2029
7/4/2029
8/4/2029
9/4/2029
10/4/2029
11/4/2029
12/4/2029
1/5/2030
2/5/2030
3/5/2030
4/5/2030
5/5/2030
6/5/2030
7/5/2030
8/5/2030
9/5/2030
10/5/2030
11/5/2030
12/5/2030
1/6/2031
2/6/2031
3/6/2031
4/6/2031
5/6/2031
6/6/2031
7/6/2031
8/6/2031
9/6/2031
10/6/2031
11/6/2031
12/6/2031
1/7/2032
2/7/2032
3/7/2032
4/7/2032
5/7/2032
6/7/2032
7/7/2032
8/7/2032
9/7/2032
10/7/2032
11/7/2032
12/7/2032
1/8/2033
2/8/2033
3/8/2033
4/8/2033
5/8/2033
6/8/2033
7/8/2033
8/8/2033
9/8/2033
10/8/2033
11/8/2033
12/8/2033
1/9/2034
2/9/2034
3/9/2034
4/9/2034
5/9/2034
6/9/2034
7/9/2034
8/9/2034
9/9/2034
10/9/2034
11/9/2034
12/9/2034
1/10/2035
2/10/2035
3/10/2035
4/10/2035
5/10/2035
6/10/2035
7/10/2035
8/10/2035
9/10/2035
10/10/2035
11/10/2035
12/10/2035
1/11/2036
2/11/2036
3/11/2036
4/11/2036
5/11/2036
6/11/2036
7/11/2036
8/11/2036
9/11/2036
10/11/2036
11/11/2036
12/11/2036
1/12/2037
2/12/2037
3/12/2037
4/12/2037
5/12/2037
6/12/2037
7/12/2037
8/12/2037
9/12/2037
10/12/2037
11/12/2037
12/12/2037
1/1/2038
2/1/2038
3/1/2038
4/1/2038
5/1/2038
6/1/2038
7/1/2038
8/1/2038
9/1/2038
10/1/2038
11/1/2038
12/1/2038
1/2/2039
2/2/2039
3/2/2039
4/2/2039
5/2/2039
6/2/2039
7/2/2039
8/2/2039
9/2/2039
10/2/2039
11/2/2039
12/2/2039
1/3/2040
2/3/2040
3/3/2040
4/3/2040
5/3/2040
6/3/2040
7/3/2040
8/3/2040
9/3/2040
10/3/2040
11/3/2040
12/3/2040
1/4/2041
2/4/2041
3/4/2041
4/4/2041
5/4/2041
6/4/2041
7/4/2041
8/4/2041
9/4/2041
10/4/2041
11/4/2041
12/4/2041
1/5/2042
2/5/2042
3/5/2042
4/5/2042
5/5/2042
6/5/2042
7/5/2042
8/5/2042
9/5/2042
10/5/2042
11/5/2042
12/5/2042
1/6/2043
2/6/2043
3/6/2043
4/6/2043
5/6/2043
6/6/2043
7/6/2043
8/6/2043
9/6/2043
10/6/2043
11/6/2043
12/6/2043
1/7/2044
2/7/2044
3/7/2044
4/7/2044
5/7/2044
6/7/2044
7/7/2044
8/7/2044
9/7/2044
10/7/2044
11/7/2044
12/7/2044
1/8/2045
2/8/2045
3/8/2045
4/8/2045
5/8/2045
6/8/2045
7/8/2045
8/8/2045
9/8/2045
10/8/2045
11/8/2045
12/8/2045
1/9/2046
2/9/2046
3/9/2046
4/9/2046
5/9/2046
6/9/2046
7/9/2046
8/9/2046
9/9/2046
10/9/2046
11/9/2046
12/9/2046
1/10/2047
2/10/2047
3/10/2047
4/10/2047
5/10/2047
6/10/2047
7/10/2047
8/10/2047
9/10/2047
10/10/2047
11/10/2047
12/10/2047
1/11/2048
2/11/2048
3/11/2048
4/11/2048
5/11/2048
6/11/2048
7/11/2048
8/11/2048
9/11/2048
10/11/2048
11/11/2048
12/11/2048
1/12/2049
2/12/2049
3/12/2049
4/12/2049
5/12/2049
6/12/2049
7/12/2049
8/12/2049
9/12/2049
10/12/2049
11/12/2049
12/12/2049
1/1/2050
2/1/2050
3/1/2050
4/1/2050
5/1/2050
6/1/2050
7/1/2050
8/1/2050
9/1/2050
10/1/2050
11/1/2050
12/1/2050
1/2/2051
2/2/2051
3/2/2051
4/2/2051
5/2/2051
6/2/2051
7/2/2051
8/2/2051
9/2/2051
10/2/2051
11/2/2051
12/2/2051
1/3/2052
2/3/2052
3/3/2052
4/3/2052
5/3/2052
6/3/2052
7/3/2052
8/3/2052
9/3/2052
10/3/2052
11/3/2052
12/3/2052
1/4/2053
2/4/2053
3/4/2053
4/4/2053
5/4/2053
6/4/2053
7/4/2053
8/4/2053
9/4/2053
10/4/2053
11/4/2053
12/4/2053
1/5/2054
2/5/2054
3/5/2054
4/5/2054
5/5/2054
6/5/2054
7/5/2054
8/5/2054
9/5/2054
10/5/2054
11/5/2054
12/5/2054
1/6/2055
2/6/2055
3/6/2055
4/6/2055
5/6/2055
6/6/2055
7/6/2055
8/6/2055
9/6/2055
10/6/2055
11/6/2055
12/6/2055
1/7/2056
2/7/2056
3/7/2056
4/7/2056
5/7/2056
6/7/2056
7/7/2056
8/7/2056
9/7/2056
10/7/2056
11/7/2056
12/7/2056
1/8/2057
2/8/2057
3/8/2057
4/8/2057
5/8/2057
6/8/2057
7/8/2057
8/8/2057
9/8/2057
10/8/2057
11/8/2057
12/8/2057
1/9/2058
2/9/2058
3/9/2058
4/9/2058
5/9/2058
6/9/2058
7/9/2058
8/9/2058
9/9/2058
10/9/2058
11/9/2058
12/9/2058
1/10/2059
2/10/2059
3/10/2059
4/10/2059
5/10/2059
6/10/2059
7/10/2059
8/10/2059
9/10/2059
10/10/2059
11/10/2059
12/10/2059
1/11/2060
2/11/2060
3/11/2060
4/11/2060
5/11/2060
6/11/2060
7/11/2060
8/11/2060
9/11/2060
10/11/2060
11/11/2060
12/11/2060
1/12/2061
2/12/2061
3/12/2061
4/12/2061
5/12/2061
6/12/2061
7/12/2061
8/12/2061
9/12/2061
10/12/2061
11/12/2061
12/12/2061
1/1/2062
2/1/2062
3/1/2062
4/1/2062
5/1/2062
6/1/2062
7/1/2062
8/1/2062
9/1/2062
10/1/2062
11/1/2062
12/1/2062
1/2/2063
2/2/2063
3/2/2063
4/2/2063
5/2/2063
6/2/2063
7/2/2063
8/2/2063
9/2/2063
10/2/2063
11/2/2063
12/2/2063
1/3/2064
2/3/2064
3/3/2064
4/3/2064
5/3/2064
6/3/2064
7/3/2064
8/3/2064
9/3/2064
10/3/2064
11/3/2064
12/3/2064
1/4/2065
2/4/2065
3/4/2065
4/4/2065
5/4/2065
6/4/2065
7/4/2065
8/4/2065
9/4/2065
10/4/2065
11/4/2065
12/4/2065
1/5/2066
2/5/2066
3/5/2066
4/5/2066
5/5/2066
6/5/2066
7/5/2066
8/5/2066
9/5/2066
10/5/2066
11/5/2066
12/5/2066
1/6/2067
2/6/2067
3/6/2067
4/6/2067
5/6/2067
6/6/2067
7/6/2067
8/6/2067
9/6/2067
10/6/2067
11/6/2067
12/6/2067
1/7/2068
2/7/2068
3/7/2068
4/7/2068
5/7/2068
6/7/2068
7/7/2068
8/7/2068
9/7/2068
10/7/2068
11/7/2068
12/7/2068
1/8/2069
2/8/2069
3/8/2069
4/8/2069
5/8/2069
6/8/2069
7/8/2069
8/8/2069
9/8/2069
10/8/2069
11/8/2069
12/8/2069
1/9/2070
2/9/2070
3/9/2070
4/9/2070
5/9/2070
6/9/2070
7/9/2070
8/9/2070
9/9/2070
10/9/2070
11/9/2070
12/9/2070
1/10/2071
2/10/2071
3/10/2071
4/10/2071
5/10/2071
6/10/2071
7/10/2071
8/10/2071
9/10/2071
10/10/2071
11/10/2071
12/10/2071
1/11/2072
2/11/2072
3/11/2072
4/11/2072
5/11/2072
6/11/2072
7/11/2072
8/11/2072
9/11/2072
10/11/2072
11/11/2072
12/11/2072
1/12/2073
2/12/2073
3/12/2073
4/12/2073
5/12/2073
6/12/2073
7/12/2073
8/12/2073
9/12/2073
10/12/2073
11/12/2073
12/12/2073
1/1/2074
2/1/2074
3/1/2074
4/1/2074
5/1/2074
6/1/2074
7/1/2074
8/1/2074
9/1/2074
10/1/2074
11/1/2074
12/1/2074
1/2/2075
2/2/2075
3/2/2075
4/2/2075
5/2/2075
6/2/2075
7/2/2075
8/2/2075
9/2/2075
10/2/2075
11/2/2075
12/2/2075
1/3/2076
2/3/2076
3/3/2076
4/3/2076
5/3/2076
6/3/2076
7/3/2076
8/3/2076
9/3/2076
10/3/2076
11/3/2076
12/3/2076
1/4/2077
2/4/2077
3/4/2077
4/4/2077
5/4/2077
6/4/2077
7/4/2077
8/4/2077
9/4/2077
10/4/2077
11/4/2077
12/4/2077
1/5/2078
2/5/2078
3/5/2078
4/5/2078
5/5/2078
6/5/2078
7/5/2078
8/5/2078
9/5/2078
10/5/2078
11/5/2078
12/5/2078
1/6/2079
2/6/2079
3/6/2079
4/6/2079
5/6/2079
6/6/2079
7/6/2079
8/6/2079
9/6/2079
10/6/2079
11/6/2079
12/6/2079
1/7/2080
2/7/2080
3/7/2080
4/7/2080
5/7/2080
6/7/2080
7/7/2080
8/7/2080
9/7/2080
10/7/2080
11/7/2080
12/7/2080
1/8/2081
2/8/2081
3/8/2081
4/8/2081
5/8/2081
6/8/2081
7/8/2081
8/8/2081
9/8/2081
10/8/2081
11/8/2081
12/8/2081
1/9/2082
2/9/2082
3/9/2082
4/9/2082
5/9/2082
6/9/2082
7/9/2082
8/9/2082
9/9/2082
10/9/2082
11/9/2082
12/9/2082
1/10/2083
2/10/2083
3/10/2083
4/10/2083
5/10/2083
6/10/2083
7/10/2083
8/10/2083
9/10/2083
10/10/2083
11/10/2083
12/10/2083
1/11/2084
2/11/2084
3/11/2084
4/11/2084
5/11/2084
6/11/2084
7/11/2084
8/11/2084
9/11/2084
10/11/2084
11/11/2084
12/11/2084
1/12/2085
2/12/2085
3/12/2085
4/12/2085
5/12/2085
6/12/2085
7/12/2085
8/12/2085
9/12/2085
10/12/2085
11/12/2085
12/12/2085
1/1/2086
2/1/2086
3/1/2086
4/1/2086
5/1/2086
6/1/2086
7/1/2086
8/1/2086
9/1/2086
10/1/2086
11/1/2086
12/1/2086
1/2/2087
2/2/2087
3/2/2087
4/2/2087
5/2/2087
6/2/2087
7/2/2087
8/2/2087
9/2/2087
10/2/2087
11/

Effect of anti-CSF-1 Ab on body weights of mice after addition of DSS (1%) in drinking water



n = 10. Antibodies injected weekly at 10mg/kg sub cut.
1st injection 24hrs before addition of 1% DSS to drinking water
Statistical analysis by ANOVA with Bonferroni's post test.
* P<0.01, *** P<0.001 101.4 vs normal animals
P<0.05, ## P<0.01, ### P<0.001 101.4 vs anti-CSF-1
No significant difference between anti-CSF-1 and normal animals

Effect of anti-CSF-1 Ab on colon length of mice after addition of DSS (1%) in drinking water for 8 days



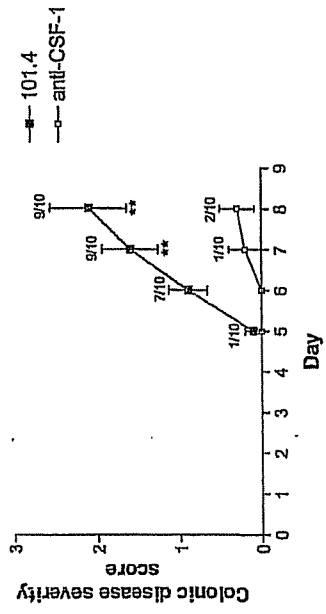
n = 10. Antibodies injected weekly at 10mg/kg sub cut.
1st injection 24hrs before addition of 1% DSS to drinking water
Statistical analysis by ANOVA with Bonferroni's post test

ASSESSED AND UNDERSTOOD: DATE: / /

INVENTED BY: DATE: / /

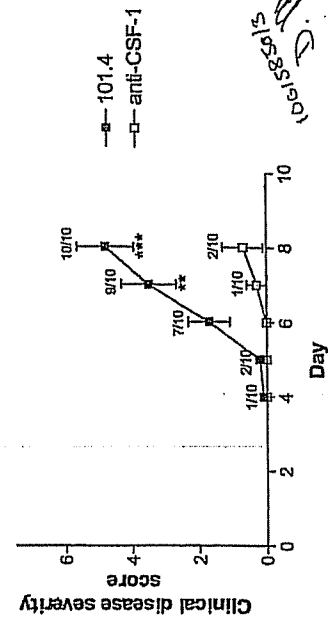
RECORDED BY: DATE: / /

Effect of anti-CSF-1 Ab on colonic disease severity score of mice after addition of DSS (1%) in drinking water



Disease scored: 1 = soft faeces/diarrhoea; 2 = signs of blood in guilfaeces;
4 = profuse bleeding from anus.
** P<0.01 analysed by Mann Whitney

Effect of anti-CSF-1 Ab on clinical disease severity score of mice after addition of DSS (1%) in drinking water



Disease scored as gut disease score plus weight loss score.
gut disease score: 1 = soft faeces/diarrhoea; 2 = signs of blood in guilfaeces;
4 = profuse bleeding from anus
weight loss score: 1 = 5-10%; 2 = 10-15%; 3 = 15-25% weight loss
** P<0.01; *** P<0.001 analysed by Mann Whitney

ASSESSED AND UNDERSTOOD: DATE: / /

INVENTED BY: DATE: / /

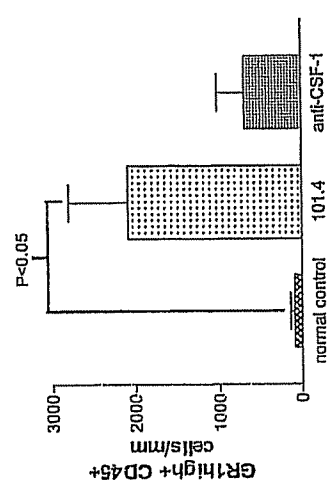
RECORDED BY: DATE: / /

DATE
PROJECT NO
NOTEBOOK NO

TITLE: anti-CSF-1

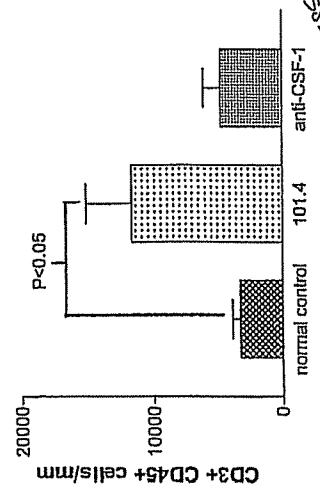
DATE
PROJECT NO
NOTEBOOK NO

GR1 high+ CD45+ cells/mm in LP population from colons of mice on day 8 after DSS (1%)



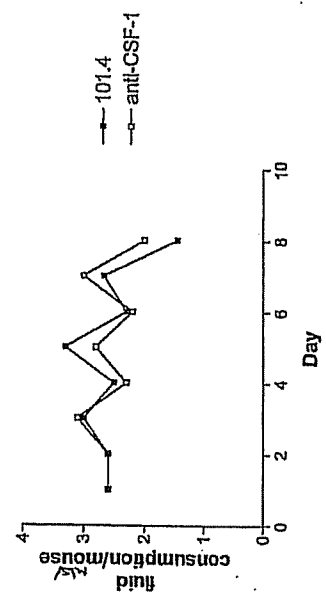
n = 10. Antibodies injected weekly at 10mg/kg sub cut.
1st injection 24hrs before addition of 1% DSS to drinking water
Statistical analysis by ANOVA with Bonferroni's post test.

CD3+ CD45+ cells/mm in LP population from colons of mice on day 8, after DSS (1%)



n = 10. Antibodies injected weekly at 10mg/kg sub cut.
1st injection 24hrs before addition of 1% DSS to drinking water
Statistical analysis by ANOVA with Bonferroni's post test.

Fluid consumption after addition of DSS (1%) in drinking water



(CSF-1) ppm Data Table-colon length

A	B	C
	anti-CSF-1	normal control
101.4	Y	Y
1	7.80	8.30
2	5.80	8.50
3	6.60	5.50
4	5.40	8.60
5	6.10	8.50
6	5.20	9.00
7	6.00	8.70
8	5.90	7.90
9	6.00	9.00
10	7.10	9.50

101.4 101.4 101.4 101.4 101.4 101.4 101.4 101.4 101.4 101.4

ASSESSED AND UNDERSTOOD BY
DATE
INVENTED BY
RECORDED BY

DATE
INVENTED BY
RECORDED BY

DATE
INVENTED BY
RECORDED BY

DATE
INVENTED BY
RECORDED BY

DATE
INVENTED BY
RECORDED BY

DATE
INVENTED BY
RECORDED BY

DATE
PROJECT NO
NOTEBOOK NO

Marina DSS - July 03.1

Cage 1 - DSS + 101.4

Fluid consumption

Day	New weight	Weight diff	Difference	Diff - 1m	Ampl per mouse (ml)
1	442	442	27	28	2.6
2	415	415	27	28	2.6
3	415	415	27	28	2.6
4	384	384	28	29	2.5
5	350	350	34	35	3.3
6	314	314	24	25	2.2
7	280	280	24	25	2.6
8	237	237	14	15	1.4
9	0	0	0	0	-1.4
10	0	0	0	0	-1.4
11	0	0	0	0	-1.4
12	0	0	0	0	-1.4
13	0	0	0	0	-1.4

Cage 2 - DSS + anti-CSF-1, AB33

Day	New weight	Weight diff	Difference	Diff - 1m	Ampl per mouse (ml)
1	404	404	27	28	2.6
2	377	377	27	28	2.6
3	345	345	32	33	3.1
4	308	308	34	35	3.3
5	267	267	23	24	2.2
6	209	209	28	29	2.6
7	163	163	18	19	1.6
8	123	123	0	0	-1.4
9	0	0	0	0	-1.4
10	0	0	0	0	-1.4
11	0	0	0	0	-1.4
12	0	0	0	0	-1.4
13	0	0	0	0	-1.4

Cage 3 - control (0 mice)

Day	New weight	Weight diff	Difference	Diff - 1m	Ampl per mouse (ml)
1	601	601	22	21	2.1
2	570	570	25	24	2.4
3	548	548	28	27	2.7
4	542	542	24	23	2.3
5	516	516	25	24	2.4
6	512	512	27	26	2.6
7	518	518	24	23	2.3
8	0	0	0	0	-1.4
9	0	0	0	0	-1.4
10	0	0	0	0	-1.4
11	0	0	0	0	-1.4
12	0	0	0	0	-1.4
13	0	0	0	0	-1.4

Cage 4 - control (1 mouse)

Day	New weight	Weight diff	Difference	Diff - 1m	Ampl per mouse (ml)
1	517	517	0	-1	-1
2	510	510	7	0	0
3	505	505	5	4	4
4	501	501	4	3	3
5	481	481	6	5	5
6	473	473	4	3	3
7	0	0	0	0	0
8	0	0	0	0	0
9	0	0	0	0	0
10	0	0	0	0	0
11	0	0	0	0	0
12	0	0	0	0	0
13	0	0	0	0	0

1005850
1005850
1005850

DATE
PROJECT NO
NOTEBOOK NO

Marina DSS - July 03.1

Cage 1 - DSS + 101.4

Day	New weight	Weight diff	Difference	Diff - 1m	Ampl per mouse (ml)
1	442	442	27	28	2.6
2	415	415	27	28	2.6
3	415	415	27	28	2.6
4	384	384	28	29	2.5
5	350	350	34	35	3.3
6	314	314	24	25	2.2
7	280	280	24	25	2.6
8	237	237	14	15	1.4
9	0	0	0	0	-1.4
10	0	0	0	0	-1.4
11	0	0	0	0	-1.4
12	0	0	0	0	-1.4
13	0	0	0	0	-1.4

Cage 2 - DSS + anti-CSF-1, AB33

Day	New weight	Weight diff	Difference	Diff - 1m	Ampl per mouse (ml)
1	404	404	27	28	2.6
2	377	377	27	28	2.6
3	345	345	32	33	3.1
4	308	308	34	35	3.3
5	267	267	23	24	2.2
6	209	209	28	29	2.6
7	163	163	18	19	1.6
8	123	123	0	0	-1.4
9	0	0	0	0	-1.4
10	0	0	0	0	-1.4
11	0	0	0	0	-1.4
12	0	0	0	0	-1.4
13	0	0	0	0	-1.4

Cage 3 - control (0 mice)

Day	New weight	Weight diff	Difference	Diff - 1m	Ampl per mouse (ml)
1	601	601	22	21	2.1
2	570	570	25	24	2.4
3	548	548	28	27	2.7
4	542	542	24	23	2.3
5	516	516	25	24	2.4
6	512	512	27	26	2.6
7	518	518	24	23	2.3
8	0	0	0	0	-1.4
9	0	0	0	0	-1.4
10	0	0	0	0	-1.4
11	0	0	0	0	-1.4
12	0	0	0	0	-1.4
13	0	0	0	0	-1.4

Cage 4 - control (1 mouse)

Day	New weight	Weight diff	Difference	Diff - 1m	Ampl per mouse (ml)
1	517	517	0	-1	-1
2	510	510	7	0	0
3	505	505	5	4	4
4	501	501	4	3	3
5	481	481	6	5	5
6	473	473	4	3	3
7	0	0	0	0	0
8	0	0	0	0	0
9	0	0	0	0	0
10	0	0	0	0	0
11	0	0	0	0	0
12	0	0	0	0	0
13	0	0	0	0	0

1005850
1005850
1005850

DATE
PROJECT NO
NOTEBOOK NO

Marina DSS - July 03.1

Cage 1 - DSS + 101.4

Day	New weight	Weight diff	Difference	Diff - 1m	Ampl per mouse (ml)
1	442	442	27	28	2.6
2	415	415	27	28	2.6
3	415	415	27	28	2.6
4	384	384	28	29	2.5
5	350	350	34	35	3.3
6	314	314	24	25	2.2
7	280	280	24	25	2.6
8	237	237	14	15	1.4
9	0	0	0	0	-1.4
10	0	0	0	0	-1.4
11	0	0	0	0	-1.4
12	0	0	0	0	-1.4
13	0	0	0	0	-1.4

Cage 2 - DSS + anti-CSF-1, AB33

Day	New weight	Weight diff	Difference	Diff - 1m	Ampl per mouse (ml)
1	404	404	27	28	2.6
2	377	377	27	28	2.6
3	345	345	32	33	3.1
4	308	308	34	35	3.3
5	267	267	23	24	2.2
6	209	209	28	29	2.6
7	163	163	18	19	1.6
8	123	123	0	0	-1.4
9	0	0	0	0	-1.4
10	0	0	0	0	-1.4
11	0	0	0	0	-1.4
12	0	0	0	0	-1.4
13	0	0	0	0	-1.4

Cage 3 - control (0 mice)

Day	New weight	Weight diff	Difference	Diff - 1m	Ampl per mouse (ml)
1	601	601	22	21	2.1
2	570	570	25	24	2.4
3	548	548	28	27	2.7
4	542	542	24	23	2.3
5	516	516	25	24	2.4
6	512	512	27	26	2.6
7	518	518	24	23	2.3
8	0	0	0	0	-1.4
9	0	0	0	0	-1.4
10	0	0	0	0	-1.4
11	0	0	0	0	-1.4
12	0	0	0	0	-1.4
13	0	0	0	0	-1.4

Cage 4 - control (1 mouse)

Day	New weight	Weight diff	Difference	Diff - 1m	Ampl per mouse (ml)
1	517	517	0	-1	-1
2	510	510	7	0	0
3	505	505	5	4	4
4	501	501	4	3	3
5	481	481	6	5	5
6	473	473	4	3	3
7	0	0	0	0	0
8	0	0	0	0	0
9	0	0	0	0	0
10	0	0	0	0	0
11	0	0	0	0	0
12	0	0	0	0	0
13	0	0	0	0	0

1005850
1005850
1005850

DATE
PROJECT NO
NOTEBOOK NO

Marina DSS - July 03.1

Cage 1 - DSS + 101.4

Day	New weight	Weight diff	Difference	Diff - 1m	Ampl per mouse (ml)
1	442	442	27	28	2.6
2	415	415	27	28	2.6
3	415	415	27	28	2.6
4	384	384	28	29	2.5
5	350	350	34	35	3.3
6	314	314	24	25	2.2
7	280	280	24	25	2.6
8	237	237	14	15	1.4
9	0	0	0	0	-1.4
10	0	0	0	0	-1.4
11	0	0	0	0	-1.4
12	0	0	0	0	-1.4
13	0	0	0	0	-1.4

Cage 2 - DSS + anti-CSF-1, AB33

Day	New weight	Weight diff	Difference	Diff - 1m	Ampl per mouse (ml)
1	404	404	27	28	2.6
2	377	377	27	28	2.6
3	345	345	32	33	3.1
4	308	308	34	35	3.3
5	267	267	23	24	2.2
6	209	209	28	29	2.6
7	163	163	18	19	1.6
8	123	123	0	0	-1.4
9	0	0	0	0	-1.4
10	0	0	0	0	-1.4
11	0	0	0	0	-1.4
12	0	0	0	0	-1.4
13	0	0	0	0	-1.4

Cage 3 - control (0 mice)

Day	New weight	Weight diff	Difference	Diff - 1m	Ampl per mouse (ml)
1	601	601	22	21	2.1
2	570	570	25	24	2.4
3	548	548	28	27	2.7
4	542	542	24	23	2.3
5	516	516	25	24	2.4
6	512	512	27	26	2.6
7	518	518	24	23	2.3
8	0	0	0	0	-1.4
9	0	0	0	0	-1.4
10	0	0	0	0	-1.4
11	0	0	0	0	-1.4
12	0	0	0	0	-1.4
13	0	0	0	0	-1.4

Cage 4 - control (1 mouse)

Day	New weight	Weight diff	Difference	Diff - 1m	Ampl per mouse (ml)
1	517	517	0	-1	-1
2	510	510	7	0	0
3	505	505	5	4	4
4	501	501	4	3	3
5	481	481	6	5	5
6	473	473	4	3	3
7	0	0	0	0	0
8	0	0	0	0	0
9	0	0	0	0	0
10	0	0	0	0	0
11	0	0	0	0	0
12	0	0	0	0	0
13	0	0	0	0	0

1005850
1

DATE
PROJECT NO
NOTEBOOK NO

TITLE: anti-CSF-1

DATE
PROJECT NO
NOTEBOOK NO

TITLE: anti-CSF-1

Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

INVENTED BY DATE
RECORDED BY DATE
ASSESSED AND UNDERSTOOD DATE

INVENTED BY DATE
RECORDED BY DATE
ASSESSED AND UNDERSTOOD DATE

REDACTED

REDACTED

TITLE: Q.1111 - CSF-1

PAGE No. 13

DATE

PROJECT NO

NOTEBOOK NO 10015859

(CSF-1) pzmResults-1: One-way ANOVA colon length: Tabular results -

X Labels		A	B	C
Parameter		Value	Data Set-B	Data Set-C
X		Y	Y	Y
1	Table Analyzed			
2	Data Table-colon length			
3	One-way analysis of variance	P<0.0001		
4	P value	***		
5	P value summary	Yes		
6	Are means signif. different? (P < 0.05)	3		
7	Number of groups	37.01		
8	F	0.7327		
9	R squared			
10				
11	Bartlett's test for equal variances			
12	Bartlett's statistic (corrected)	7.186		
13	P value	0.0275		
14	P value summary	Yes		
15	Do the variances differ signif. (P < 0.05)			
16				
17	ANOVA Table	SS	df	MS
18	Treatment (between columns)	55.71	2	27.86
19	Residual (within columns)	20.32	27	0.7527
20	Total	76.04	29	
21				
22	Bonferroni's Multiple Comparison Test	Mean Diff.	t	P value
23	101.4 vs anti-CSF-1	-1.960	5.052	F < 0.001
24	101.4 vs normal control	-3.320	8.557	P < 0.001
25	anti-CSF-1 vs normal control	-1.360	3.505	P < 0.01

1001585913

ASSESSED AND UNDERSTOOD

DATE

INVENTED BY

DATE

BY

RECORDED BY

DATE

ASSESSED AND UNDERSTOOD

DATE

INVENTED BY

DATE

RECORDED BY

DATE

TITLE: Q.1111 - CSF-1

PAGE No. 13

DATE

PROJECT NO

NOTEBOOK NO 10015859

(CSF-1) pzmResults-3: One-way ANOVA d4 weights: Tabular results -

X Labels		A	B	C	D
Parameter		Value	Data Set-B	Data Set-C	Data Set-D
X		Y	Y	Y	Y
1	Table Analyzed				
2	Data Table-5 weights table for stats				
3	One-way analysis of variance				
4	P value	0.0074			
5	P value summary	**			
6	Are means signif. different? (P < 0.05)	Yes			
7	Number of groups	3			
8	F	5.908			
9	R squared	0.3044			
10					
11	Bartlett's test for equal variances				
12	Bartlett's statistic (corrected)	1.710			
13	P value	0.4254			
14	P value summary	ns			
15	Do the variances differ signif. (P < 0.05)	No			
16					
17	ANOVA Table	SS	df	MS	
18	Treatment (between columns)	52.42	2	26.21	
19	Residual (within columns)	119.8	27	4.438	
20	Total	172.2	29		
21					
22	Bonferroni's Multiple Comparison Test	Mean Diff.	t	P value	95% CI of diff
23	control,d4 vs csf,d4	1.144	1.214	P > 0.05	-1.261 to 3.548
24	control,d4 vs 101,d4	3.195	3.392	P < 0.01	0.7908 to 5.599
25	csf,d4 vs 101,d4	2.052	2.178	P > 0.05	-0.3527 to 4.456

1001585913

1001585913

REDACTED

REDACTED

(CSF-1) pzmResults-5One-way ANOVA (and nonparametric) Tabular results - Two data sets

X Labels Parameter	A Value	B Data Set-B	C Data Set-C	D Data Set-D
1 Table Analyzed	Y	Y	Y	Y
2 Data Table-6, weights table for stats				
3 One-way analysis of variance				
4 P value	P<0.0001			
5 P value summary	**			
6 Are means signif. different? (P < 0.05)	Yes			
7 Number of groups	3			
8 F	14.00			
9 R squared	0.5091			
10				
11 Bartlett's test for equal variances				
12 Bartlett's statistic (corrected)	9.656			
13 P value	0.0080			
14 P value summary	**			
15 Do the variances differ signif. (P < 0.05)	Yes			
16				
17 ANOVA Table	SS	df	MS	
18 Treatment (between columns)	451.5	2	225.8	
19 Residual (within columns)	435.4	27	16.13	
20 Total	886.9	29		
21				
22 Bonferroni's Multiple Comparison Test	Mean Diff.	t	P value	95% CI of diff
23 control,d5 vs csl,d6	2.160	1.203	P > 0.05	-2.424 to 6.743
24 control,d6 vs 101,d8	9.054	5.064	P < 0.001	4.510 to 13.68
25 csl,d6 vs 101,d8	6.934	3.861	P < 0.01	2.351 to 11.52

10015850115

ASSESSED AND UNDERSTOOD DATE INVENTED BY RECORDED BY DATE

(CSF-1) pzmResults-4One-way ANOVA d5 weights Tabular results - Two data sets

X Labels Parameter	A Value	B Data Set-B	C Data Set-C	D Data Set-D
1 Table Analyzed	Y	Y	Y	Y
2 Data Table-6, weights table for stats				
3 One-way analysis of variance				
4 P value	0.0028			
5 P value summary	**			
6 Are means signif. different? (P < 0.05)	Yes			
7 Number of groups	3			
8 F	7.364			
9 R squared	0.3530			
10				
11 Bartlett's test for equal variances				
12 Bartlett's statistic (corrected)	4.763			
13 P value	0.0915			
14 P value summary	ns			
15 Do the variances differ signif. (P < 0.05)	No			
16				
17 ANOVA Table	SS	df	MS	
18 Treatment (between columns)	104.5	2	52.25	
19 Residual (within columns)	191.6	27	7.095	
20 Total	296.0	29		
21				
22 Bonferroni's Multiple Comparison Test	Mean Diff.	t	P value	95% CI of diff
23 control,d5 vs csl,d5	1.262	1.059	P > 0.05	-1.779 to 4.302
24 control,d5 vs 101,d5	4.436	3.724	P < 0.01	1.396 to 7.477
25 csl,d5 vs 101,d5	3.174	2.685	P < 0.05	0.1340 to 6.215

10015850114

ASSESSED AND UNDERSTOOD DATE INVENTED BY RECORDED BY DATE

REDACTED

REDACTED

DATE
PROJECT NO
NOTEBOOK NO

(CSF-1) pm-Results-7 One-way ANOVA (and nonparametric) Tabular results -

X Labels Parameter	A		B		C		D	
	Value		Data Set-B		Data Set-C		Data Set-D	
1 Table Analyzed	Y		Y		Y		Y	
2 Data Table-5, weights table for stats								
3 One-way analysis of variance								
4 P value	P<0.0001							
5 P value summary	**							
6 Are means signif. different? (P < 0.05)	Yes							
7 Number of groups	3							
8 F	22.18							
9 R squared	0.6216							
10								
11 Bartlett's test for equal variances								
12 Bartlett's statistic (corrected)	6.455							
13 P value	0.0397							
14 P value summary	*							
15 Do the variances differ signif. (P < 0.05)	Yes							
16								
17 ANOVA Table	SS		df		MS			
18 Treatment (between columns)	2144		2		1072			
19 Residual (within columns)	1305		27		48.34			
20 Total	3449		29					
21								
22 Bonferroni's Multiple Comparison Test	Mean Diff.		t		P value		95% CI of diff	
23 control,d8 vs csf,d8	5.065		1.629		P > 0.05		-2.871 to 13.00	
24 control,d8 vs 101,d8	19.92		6.407		P < 0.001		11.59 to 27.86	
25 csf,d8 vs 101,d8	14.86		4.778		P < 0.001		6.920 to 22.79	

10015850117

DATE
PROJECT NO
NOTEBOOK NO

(CSF-1) pm-Results-8 One-way ANOVA (and nonparametric) Tabular results -

X Labels Parameter	A		B		C		D	
	Value		Data Set-B		Data Set-C		Data Set-D	
1 Table Analyzed	Y		Y		Y		Y	
2 Data Table-5, weights table for stats								
3 One-way analysis of variance								
4 P value	P<0.0001							
5 P value summary	**							
6 Are means signif. different? (P < 0.05)	Yes							
7 Number of groups	3							
8 F	25.98							
9 R squared	0.6581							
10								
11 Bartlett's test for equal variances								
12 Bartlett's statistic (corrected)	13.91							
13 P value	0.0010							
14 P value summary	**							
15 Do the variances differ signif. (P < 0.05)	Yes							
16								
17 ANOVA Table	SS		df		MS			
18 Treatment (between columns)	1319		2		659.6			
19 Residual (within columns)	665.4		27		25.39			
20 Total	2005		29					
21								
22 Bonferroni's Multiple Comparison Test	Mean Diff.		t		P value		95% CI of diff	
23 control,d7 vs csf,d7	4.164		1.848		P > 0.05		-1.588 to 9.915	
24 control,d7 vs 101,d7	15.68		6.958		P < 0.001		9.928 to 21.43	
25 csf,d7 vs 101,d7	11.52		5.110		P < 0.001		5.764 to 17.27	

10015850116

ASSESSED AND UNDERSTOOD DATE
INVENTED BY DATE
RECORDED BY DATE

ASSESSED AND UNDERSTOOD DATE
INVENTED BY DATE
RECORDED BY DATE

REDACTED

REDACTED

TITLE: 0001-035F-1

PAGE No. 18

DATE

PROJECT NO

NOTEBOOK NO : 10015850

(CSF-1) pzmResults-121 tests (and nonparametric test) Tabular results -

X Labels		A
Parameter	Value	
X		Y
1 Table Analyzed		Data Table-colonic disease score for stats
2		
3 Mann Whitney test		
4 P value		0.0021
5 Exact or approximate P value?		Gaussian Approximation
6 P value summary		**
7 Are medians signif. different? (P < 0.05)		Yes
8 One- or two-tailed P value?		Two-tailed
9 Sum of ranks in column C,G		143.5 , 66.50
10 Mann-Whitney U		11.50

10015850/18

(CSF-1) pzmResults-121 tests (and nonparametric test) Tabular results -

X Labels		A
Parameter	Value	
X		Y
1 Table Analyzed		Data Table-colonic disease score for stats
2		
3 Mann Whitney test		
4 P value		0.0029
5 Exact or approximate P value?		Gaussian Approximation
6 P value summary		**
7 Are medians signif. different? (P < 0.05)		Yes
8 One- or two-tailed P value?		Two-tailed
9 Sum of ranks in column D,H		143 , 67
10 Mann-Whitney U		12.00

10015850/18

ASSESSED AND UNDERSTOOD

DATE

DATE

BY

INVENTED BY

DATE

RECORDED BY

DATE

TITLE: 0001-035F-1

PAGE No. 19

DATE

PROJECT NO

NOTEBOOK NO : 10015850

(CSF-1) pzmResults-141 tests (and nonparametric test) Tabular results -

X Labels		A
Parameter	Value	
X		Y
1 Table Analyzed		Data Table-clinical disease score for stats
2		
3 Mann Whitney test		
4 P value		0.0011
5 Exact or approximate P value?		Gaussian Approximation
6 P value summary		**
7 Are medians signif. different? (P < 0.05)		Yes
8 One- or two-tailed P value?		Two-tailed
9 Sum of ranks in column D,I		146 , 64
10 Mann-Whitney U		9.000

10015850/19

(CSF-1) pzmResults-141 tests (and nonparametric test) Tabular results -

X Labels		A
Parameter	Value	
X		Y
1 Table Analyzed		Data Table-clinical disease score for stats
2		
3 Mann Whitney test		
4 P value		0.0003
5 Exact or approximate P value?		Gaussian Approximation
6 P value summary		**
7 Are medians signif. different? (P < 0.05)		Yes
8 One- or two-tailed P value?		Two-tailed
9 Sum of ranks in column E,J		146.5 , 61.50
10 Mann-Whitney U		6.500

10015850/19

ASSESSED AND UNDERSTOOD

DATE

INVENTED BY

DATE

BY

RECORDED BY

DATE

TITLE: anti-CSF-1

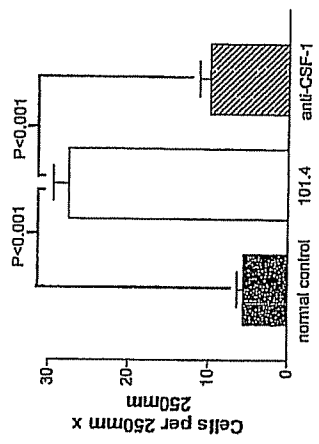
PAGE No. 2
DATE
PROJECT NO
NOTEBOOK NO 10015850

TITLE: anti-CSF-1

PAGE No. 23
DATE
PROJECT NO
NOTEBOOK NO 10015850

CD3⁺ cell counts by immunohistochemistry from Jones Camaron

CD3⁺ cell count from colons of mice on day 8, after DSS (1%)



n = 10. Antibodies injected weekly at 10mg/kg sub cul.
1st injection 24hrs before addition of 1% DSS to drinking water
Statistical analysis by ANOVA with Bonferroni's post test.
10015850/22

CD3⁺ cell counts by immunohistochemistry from Jones Camaron

Block No.	Animal No.	Counts	
887-03	101.4 gp 1.1	22	23
888-03	101.4 gp 1.2	22	18
889-03	101.4 gp 1.3	41	64
890-03	101.4 gp 1.4	17	21
891-03	101.4 gp 1.5	18	29
892-03	101.4 gp 1.6	39	36
893-03	101.4 gp 1.7	39	36
894-03	101.4 gp 1.8	14	20
895-03	101.4 gp 1.9	31	30
896-03	101.4 gp 2.1	6	9
897-03	ab 33 gp 2.2	9	8
898-03	ab 33 gp 2.3	18	15
899-03	ab 33 gp 2.4	15	9
900-03	ab 33 gp 2.5	1	9
901-03	ab 33 gp 2.6	8	11
902-03	ab 33 gp 2.7	18	21
903-03	ab 33 gp 2.8	10	13
904-03	ab 33 gp 2.9	12	13
905-03	ab 33 gp 2.10	2	3
906-03	normal gp3.1	7	8
907-03	normal gp3.2	3	5
908-03	normal gp3.3	5	10
909-03	normal gp3.4	4	7
910-03	normal gp3.5	3	3
911-03	normal gp3.6	1	2
912-03	normal gp3.7	12	10
913-03	normal gp3.8	1	7
914-03	normal gp3.9	5	4
915-03	normal gp3.10	15	10
916-03	normal gp3.10	15	10

10015850/23

ASSESSED AND UNDERSTOOD
BY
DATE
INVENTED BY
DATE
RECORDED BY
DATE

ASSESSED AND UNDERSTOOD
DATE
INVENTED BY
DATE
RECORDED BY
DATE

REDACTED

REDACTED

TITLE: anti-CSF-1

PAGE No. 25

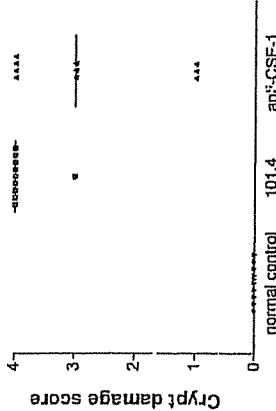
DATE

PROJECT NO

NOTEBOOK NO 10015850

Histological crypt damage
score from colons of mice on
day 8 after administration of
DSS

By ANOVA anti-CSF-1
treatment lead to less
histological crypt damage
than mice with DSS
colons are mentioned
with 101.4



101.4 anti-CSF-1

10015850/24

Block No.	Animal No.	Damage
887-03	101.4 gp 1.1	3
888-03	101.4 gp 1.2	4
889-03	101.4 gp 1.3	4
890-03	101.4 gp 1.4	4
891-03	101.4 gp 1.5	4
892-03	101.4 gp 1.6	4
893-03	101.4 gp 1.7	4
894-03	101.4 gp 1.8	4
895-03	101.4 gp 1.9	4
896-03	101.4 gp 1.10	4
897-03	ab 33 gp 2.1	3
898-03	ab 33 gp 2.2	1
899-03	ab 33 gp 2.3	4
900-03	ab 33 gp 2.4	4
901-03	ab 33 gp 2.5	4
902-03	ab 33 gp 2.6	1
903-03	ab 33 gp 2.7	4
904-03	ab 33 gp 2.8	4
905-03	ab 33 gp 2.9	3
906-03	ab 33 gp 2.10	1
907-03	normal gp3.1	0
908-03	normal gp3.2	0
909-03	normal gp3.3	0
910-03	normal gp3.4	0
911-03	normal gp3.5	0
912-03	normal gp3.6	0
913-03	normal gp3.7	0
914-03	normal gp3.8	0
915-03	normal gp3.9	0
916-03	normal gp3.10	0

10015850/24

ASSESSED AND UNDERSTOOD

DATE

INVENTED BY

DATE

BY

RECORDED BY

DATE

ASSESSED AND UNDERSTOOD

DATE

INVENTED BY

DATE

BY

RECORDED BY

DATE

TITLE: anti-CSF-1

PAGE No. 25

DATE

PROJECT NO

NOTEBOOK NO 10015850

CSF-1 damage score pzm:Results:3:One-way ANOVA (and nonparametric) Tabular results

X Labels	A	B	C	D
Parameter	Value	Data Set-B	Data Set-C	Data Set-D
X	Y	Y	Y	Y
1 Table Analyzed				
2 Data Table-1				
3 One-way analysis of variance				
4 P value	P<0.0001			
5 P value summary	***			
6 Are means signif. different? (P < 0.05)	Yes			
7 Number of groups	3			
8 F	66.16			
9 R squared	0.8305			
10				
11 Bartlett's test for equal variances				
12 Bartlett's statistic (corrected)				
13 P value	ns			
14 P value summary	No			
15 Do the variances differ signif. (P < 0.05)				
16				
17 ANOVA Table	SS	df	MS	
18 Treatment (between columns)	80.87	2	40.43	
19 Residual (within columns)	16.50	27	0.6111	
20 Total	97.37	29		
21				
22 Bonferroni's Multiple Comparison Test	Mean Diff.	t	P value	95% CI of diff
23 101.4 vs anti-CSF-1	1.100	3.146	P < 0.05	0.2077 to 1.992
24 101.4 vs normal control	3.900	11.16	P < 0.001	3.006 to 4.792
25 anti-CSF-1 vs normal control	2.800	8.009	P < 0.001	1.908 to 3.692

10015850/24

REDACTED

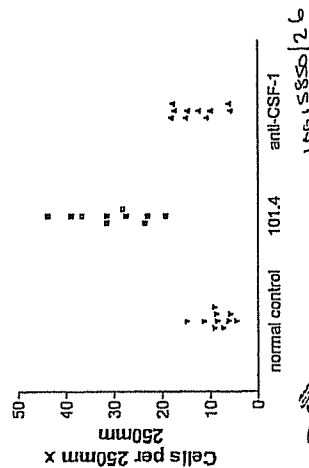
DATE

PROJECT NO

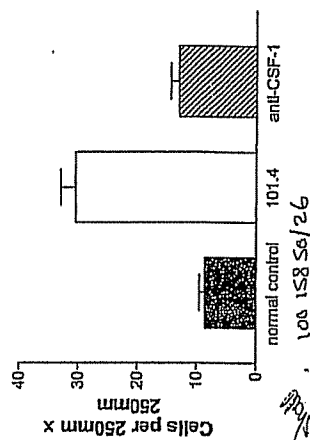
NOTEBOOK NO

10515850

F4/80+ cell count from colons
of mice on day 8, after DSS
(1%)



F4/80+ cell count from colons
of mice on day 8, after DSS
(1%)



Wij Anwar
Rafiq's post box
Wij Anwar
Wij Anwar
Wij Anwar
Wij Anwar
Wij Anwar

DATE

PROJECT NO

NOTEBOOK NO

10515850

1-4/80+ cell count

Block No.	Animal No.	Counts
887-03	101.4 gp 1.1	16
888-03	101.4 gp 1.2	21
889-03	101.4 gp 1.3	27
890-03	101.4 gp 1.4	14
891-03	101.4 gp 1.5	28
892-03	101.4 gp 1.6	37
893-03	101.4 gp 1.7	28
894-03	101.4 gp 1.8	38
895-03	101.4 gp 1.9	29
896-03	101.4 gp 1.10	20
897-03	ab 33 gp 2.1	10
898-03	ab 33 gp 2.2	7
899-03	ab 33 gp 2.3	10
900-03	ab 33 gp 2.4	12
901-03	ab 33 gp 2.5	9
902-03	ab 33 gp 2.6	9
903-03	ab 33 gp 2.7	15
904-03	ab 33 gp 2.8	7
905-03	ab 33 gp 2.9	20
906-03	ab 33 gp 3.0	9
907-03	normal gp 3.1	13
908-03	normal gp 3.2	6
909-03	normal gp 3.3	14
910-03	normal gp 3.4	7
911-03	normal gp 3.5	5
912-03	normal gp 3.6	5
913-03	normal gp 3.7	12
914-03	normal gp 3.8	5
915-03	normal gp 3.9	4
916-03	normal gp 3.10	6

10515850/27

ASSESSED AND UNDERSTOOD

DATE

INVENTED BY

DATE

BY

RECORDED BY

DATE

DATE

ASSESSED AND UNDERSTOOD

DATE

INVENTED BY

DATE

BY

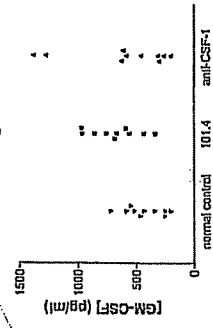
RECORDED BY

DATE

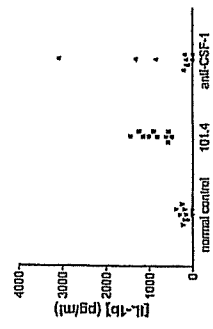
DATE

DATE

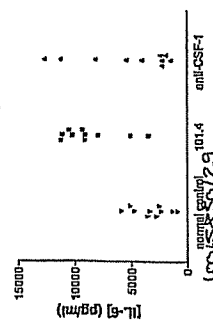
GM-CSF concentrations in mouse colon culture supernatants following administration of 1% DSS in drinking water



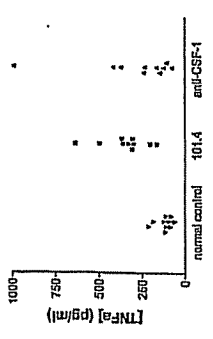
IL-1b concentrations in mouse colon culture supernatants following administration of 1% DSS in drinking water



IL-6 concentrations in mouse colon culture supernatants following administration of 1% DSS in drinking water



TNFa concentrations in mouse colon culture supernatants following administration of 1% DSS in drinking water



The anti-CSF-1 antibody is tending to decrease cytokine release into supernatant, but this is not statistically significant.

(CSF-1) (480, 480) Results: 1-One-way ANOVA (and nonparametric); Tabular results - Two-Way ANOVA

X Labels		A	B	C	D
Parameter	Value	Data Set-A	Data Set-B	Data Set-C	Data Set-D
1 Table Analyzed	Y	Y	Y	Y	Y
2 Data Table-1					
3 One-way analysis of variance					
4 P value	P<0.0001				
5 P value summary	***				
6 Are means signif. different? (P<0.05)	Yes				
7 Number of groups	3				
8 F	45.14				
9 R squared	0.7698				
10					
11 Bartlett's test for equal variances					
12 Bartlett's statistic (corrected)	7.422				
13 P value	0.0244				
14 P value summary	*				
15 Do the variances differ signif. (P<0.05)	Yes				
16					
17 ANOVA Table	SS	df	MS		
18 Treatment (between columns)	2686	2	1343		
19 Residual (within columns)	803.4	27	29.76		
20 Total	3490	29			
21					
22 Bonferroni's Multiple Comparison Test	Mean Diff.		P value	95% CI of diff	
23 101.4 vs anti-CSF-1	17.56	7.196	P<0.001	11.33 to 23.78	
24 101.4 vs normal control	21.89	8.971	P<0.001	15.66 to 28.11	
25 anti-CSF-1 vs normal control	4.330	1.775	P>0.05	-1.897 to 10.56	

1881859178

REDACTED

TITLE: C-101-051-1

PAGE No.

DATE

PROJECT NO

NOTEBOOK NO

CALCULATED CONCENTRATION

GROSS	1	2	3	4	5	6	7	8	9	10	11	12
A	459.73	278.22	189.81	89.77	59.78	59.78	59.78	59.78	59.78	59.78	59.78	59.78
B	316.19	301.00	175.93	50.75	25.48	50.75	50.75	50.75	50.75	50.75	50.75	50.75
C	31.77	194.46	161.94	31.53	8.97	31.53	31.53	31.53	31.53	31.53	31.53	31.53
D	194.48	151.81	75.576	59.803	0	59.803	59.803	59.803	59.803	59.803	59.803	59.803
E	251.54	329.45	91.204	44.815	0	91.204	91.204	91.204	91.204	91.204	91.204	91.204
F	166.39	365.62	87.212	8.97	0	87.212	87.212	87.212	87.212	87.212	87.212	87.212
G	567.63	271.3	140.55	0	0	140.55	140.55	140.55	140.55	140.55	140.55	140.55
H	281.85	238.05	52.388	0	0	52.388	52.388	52.388	52.388	52.388	52.388	52.388
L-beta												
A	720.43	645.35	165.47	645.35	645.35	645.35	645.35	645.35	645.35	645.35	645.35	645.35
B	465.83	165.47	217.89	639.28	921.26	1141.1	217.89	165.47	165.47	165.47	165.47	165.47
C	527.18	165.47	124.6	51.38	688.02	588.07	165.47	165.47	165.47	165.47	165.47	165.47
D	601.73	121.6	121.4	608.12	614.47	1018	1314.4	286.06	0	246.83	0	246.83
E	848.94	147.26	1009.7	620.75	1005.5	614.47	147.26	217.86	380.47	0	0	0
F	1440.5	340.27	512.06	814.68	768.75	819.65	147.26	165.47	0	0	0	0
G	555.26	0	1129	1278.1	620.75	805.71	57.205	165.47	0	0	0	0
H	1300.9	97.705	534.32	779.16	402.51	555.26	3889	147.26	0	0	0	0
IL-5												
A	6874	3523	2540.5	288.14	5052	10200	8128.7	8128.7	8128.7	8128.7	8128.7	8128.7
B	3760.4	1552.7	655.45	241.97	276.21	5984.1	2784.9	5409.9	5409.9	5409.9	5409.9	5409.9
C	1041.9	2215.8	1877.9	186.43	255.85	5976.5	2241.7	7225	7225	7225	7225	7225
D	2565.8	1799	0	241.97	255.27	11100	12600	2357.5	2357.5	2357.5	2357.5	2357.5
E	3300.8	1559.1	641.13	288.14	325.13	10500	1803.1	2418.7	2418.7	2418.7	2418.7	2418.7
F	2020.3	771.47	558.84	272.14	263.83	11200	1442.3	1311.6	1311.6	1311.6	1311.6	1311.6
G	6121.9	1950.8	138.8	368.37	272.14	9310.2	4042.2	5109	5109	5109	5109	5109
H	6398.4	722.09	208.11	292.02	3475.8	7933.4	11200	5930.8	5930.8	5930.8	5930.8	5930.8
TNF-alpha												
A	288.16	212.25	73.427	164.36	101.91	379.58	358.73	213.34	81.908	81.908	81.908	81.908
B	119.98	81.908	49.284	148.07	103.76	631.99	295.38	372.26	174.46	174.46	174.46	174.46
C	107.84	81.908	63.656	135.79	124.22	165.04	105.85	124.22	124.22	124.22	124.22	124.22
D	254.83	49.284	137.38	179.38	84.728	288.14	417.41	214.43	91.77	91.77	91.77	91.77
E	113.52	81.908	282.98	129.29	117.16	380.15	165.38	86.867	34.38	34.38	34.38	34.38
F	169.05	63.656	197.56	138.95	95.628	394.92	146.59	62.445	0	0	0	0
G	252.99	86.867	219.82	171.69	103.91	495.74	76.878	113.52	0	0	0	0
H	233.34	52.955	155.33	117.18	204.44	309	988.04	113.52	0	0	0	0

1,1-1,10 146-248
2,1-2,10 88-219
3,1-3,10 89-210

Analysis performed by B.C. using R+D reagents

ASSESSED AND UNDERSTOOD

DATE

INVENTED BY

DATE

REDACTED

RECORDED BY

DATE

TITLE: Anti-CSF-1 in DSS-colitis in mice

PAGE No. 53

DATE

PROJECT NO

NOTEBOOK NO 15015350

DSS model of IBD (mice)

Aim

To assess the effects of anti-CSF-1 antibody on DSS induced colitis in mice.

Procedure

Licence 70/5748, procedure 19.

Balb/c mice (males, batch RM3326, arrived 18-22/8) weighed and injected subcutaneously with mAb @ 10mg/kg.

Group 1 - 101.4, control antibody (lot- 10014426215) - (Y1 isotype)

Group 2 - Anti-CSF-1, alkylated Ab33 (4.7mg/kg) - (Y1 isotype)

10 mice in each group. Normal drinking water then replaced with 1% DSS (ICN MW 36-50K, Cat No 160110) in tap water 24 hours after 1st antibody injection. Lot no. 4377F

Group 3 - No treatment control group

10 mice will continue to have normal drinking water.

Mice will receive antibody once a week. Animals will be weighed each day and signs of disease (loose stools, bleeding) noted. The volume of 1% DSS or water consumed also measured by weight. At end of expt., colons will be removed and length measured. A 1 cm section will be collected from the distal end for assessment of neutrophil and T cell infiltration by FACS analysis. The next 2 cm section will be collected and placed in formalin for histological analysis. The next cm will be placed in culture medium for 24 hours, after which time the supernatant will be collected and cytokine levels measured by luminex. Plasma will also be collected at termination.

Not Read
Study Period

10015850/53

This experiment is an exact repeat of the experiment on 4 this boat.

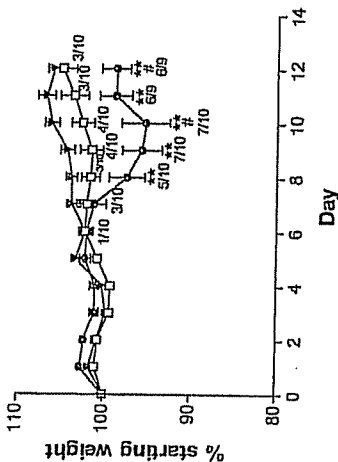
Disease incidence was low in this expt, however the anti-CSF-1 antibody does seem to again protect from weight loss, although there was no significant difference between the 101.4 vs. anti-CSF-1 groups until day 10.

ASSESSED AND UNDERSTOOD BY	DATE	INVENTED BY	DATE
		RECORDED BY	DATE

REJECTED
REJECTED

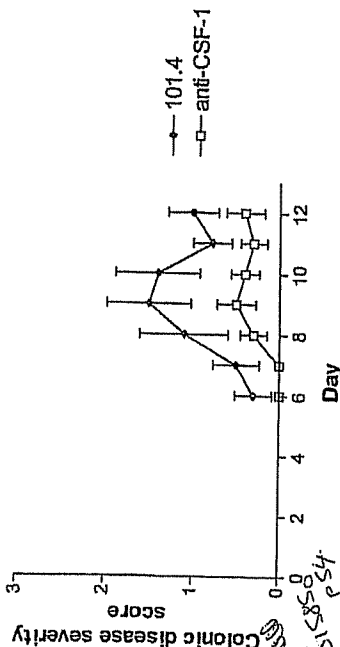
TITLE: Anti-CSF-1 in DSS - colitis in mice (2)

Effect of anti-CSF-1 Ab on body weight of mice after addition of DSS (1%) in drinking water



Antibodies injected weekly at 10mg/kg sub cut, 1st injection 24hrs before addition of 1% DSS to drinking water
Statistical analysis by ANOVA with Bonferroni's post test:
** $P < 0.01$ 101.4 vs normal animals, # $P < 0.05$ 101.4 vs anti-CSF-1
No significant difference between anti-CSF-1 and normal animals

Effect of anti-CSF-1 Ab on colonic disease severity score of mice after addition of DSS (1%) in drinking water



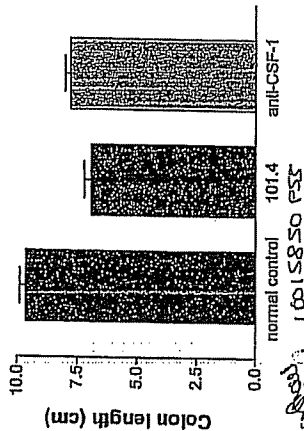
ASSESSED AND UNDERSTOOD BY: DATE: INVENTED BY: DATE: RECORDED BY: DATE:

PAGE No. 55

DATE: PROJECT NO: NOTEBOOK NO: 10015850

TITLE: Anti-CSF-1 (2)

Effect of anti-CSF-1 Ab on colon length of mice after addition of DSS (1%) in drinking water for 8 days



mice (CSF-1.2) pzmcDat

A	B	C
anti-CSF-1	101.4	normal control
Y	Y	Y
1	7.70	7.80
2	7.90	6.20
3	7.10	7.20
4	8.00	7.40
5	8.80	8.30
6	8.80	6.80
7	8.80	7.00
8	8.80	8.80
9	8.30	6.80
10	7.80	4.80

10015850 p55

ASSESSED AND UNDERSTOOD BY: DATE: INVENTED BY: DATE: RECORDED BY: DATE:

REDACTED

REDACTED

TITLE: Anti-CSF-1 (2)

PAGE No. 59

DATE

PROJECT NO

NOTEBOOK NO 10015850

mice (CSF-1/2)pmData Table-3, disease

A										
anti-CSF-1										
Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10	
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0

10015850/58

mice (CSF-1/2)pmData Table-3, disease

B										
101.4										
Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10	
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4

10015850/58

PAGE No. 59

DATE

PROJECT NO

NOTEBOOK NO 10015850

mice (CSF-1/2)pmData Table-3, disease

A										
anti-CSF-1										
Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10	
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0

10015850/58

mice (CSF-1/2)pmData Table-3, disease

B										
101.4										
Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10	
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4

10015850/58

TITLE: Anti-CSF-1 (2)

PAGE No. 59

DATE

PROJECT NO

NOTEBOOK NO 10015850

mice (CSF-1/2)pmResults-1One-way ANOVA (end nonparametric)Tabular results

X Labels		A		B		C	
Parameter		Value		Data Set-B		Data Set-C	
X		Y		Y		Y	
1	Table Analyzed						
2	Data Table-2: colon length						
3	One-way analysis of variance						
4	P value		P<0.0001				
5	P value summary		***				
6	Are means signif. different? (P < 0.05)		Yes				
7	Number of groups		3				
8	F		27.82				
9	R squared		0.6733				
10							
11	Bartlett's test for equal variances						
12	Bartlett's statistic (corrected)		0.5763				
13	P value		0.7489				
14	P value summary		ns				
15	Do the variances differ signif. (P < 0.05)		No				
16							
17	ANOVA Table		SS		df		MS
18	Treatment (between columns)		38.59		2		19.30
19	Residual (within columns)		18.73		27		0.6936
20	Total		57.32		29		
21							
22	Bonferroni's Multiple Comparison Test		Mean Diff.		t		P value
23	anti-CSF-1 vs 101.4		0.8700		2.356		P > 0.05
24	anti-CSF-1 vs normal control		-1.850		4.987		P < 0.001
25	101.4 vs normal control		-2.720		7.303		P < 0.001

10015850/59

ASSESSED AND UNDERSTOOD

DATE

INVENTED BY

DATE

BY

ASSESSED AND UNDERSTOOD

DATE

INVENTED BY

DATE

RECORDED BY

DATE

RECORDED BY

DATE

BY

RECORDED BY

DATE

RECORDED BY

DATE

DATE

DATE _____
PROJECT NO _____
NOTEBOOK NO _____

DSS model of IBD (nice).

Aim

To assess the effects of anti-CSF-1 antibody on DSS induced colitis in mice,

Procedure

Procedure
Licence 70/5748, procedure 19.
Bulbimice (mules, batch RM3357, arrived 20-25g) weighed and injected subcutaneously with mAb @: 10mg/kg.

Group I - 101.4, control antibody (lot: 10014426/15) - (γ1 isotype) twice a week

Group 2 - 101.4, control antibody (lot:- 10014426/15) - (Y1 isotype) once a week

Group 4 -- Anti-CSF-1, alkylated Ab33 (4.7mg/ml) twice a week

Group 5 -- Anti-CSF-1, alkylated Ab33 (4.7mg/ml) once a week

4379F

10 mice in each group. Normal drinking water then replaced with 1% DSS (ICN MW 36-50K, Cal No 66110) in tap water 24 hours after 1st antibody injection.

Group 3 – No treatment control group

10 mice will continue to have normal drinking water.

Mice will receive antibody once a week. Animals will be weighed each day and signs of disease (toxicity, bleeding) noted. The volume of 1% DSS or water consumed also measured by weight. At end of expt., colons will be removed and length measured. A 1 cm section will be collected from the distal end for assessment of neutrophil and T cell infiltration by FACS analysis. The next 2 cm section will be collected and placed in formalin for histological analysis. Plasma will also be collected at termination.

Study Period

07/05851991

Very severe disease was noted in this experiment, which the anti-CSI-1 failed to inhibit. Therefore it appears that the anti-CSI-1 can inhibit mild disease in OSS administered mice, but not severe disease.

Row 200750

ASSESSED AND UNDERSTOOD

DATE _____

INVENTED BY:

DATE: _____

INVENTED BY	DATE
RECORDED BY <i>D. Wilson</i>	DATE

DATE: _____
DATE: _____

ASSESSED AND UNDERSTOOD

DATE _____

INVENTED BY:

DATE _____

INVENTED BY	DATE
RECORDED BY <i>Macall</i>	DATE

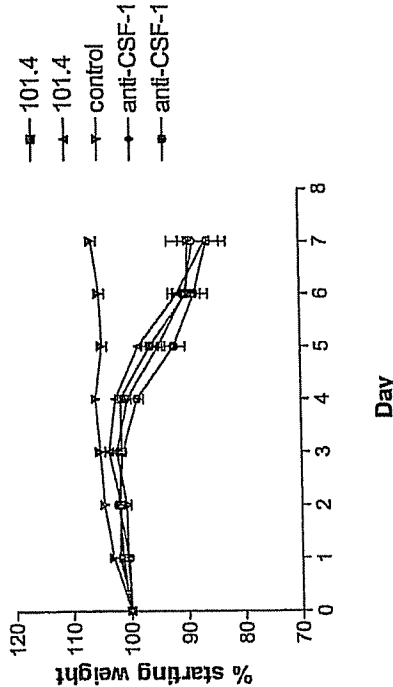
DATE _____ DATE _____

19/05850/66

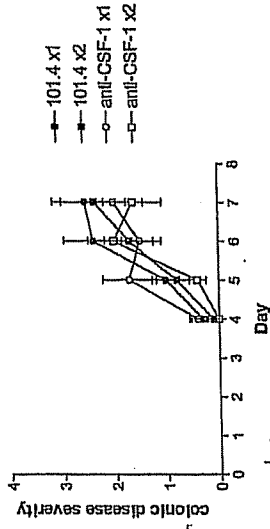
DATE
PROJECT NO
NOTEBOOK NO

$f(x) = 457 - 19x$

Effect of anti-CSF-1 Ab on colon length of mice after addition of DSS (1%) in drinking water for 7 days



Effect of anti-CSF-1 Ab on colonic disease of mice after addition of DSS (1%) in drinking water for 7 days

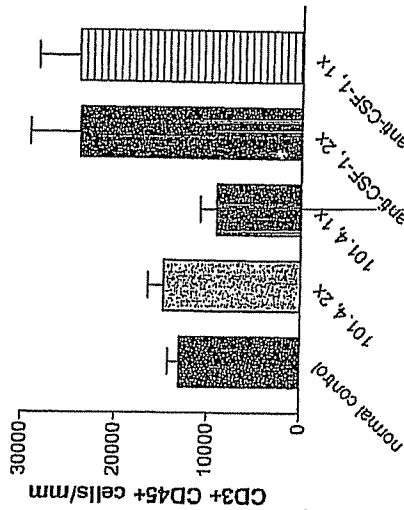


EDUCATED

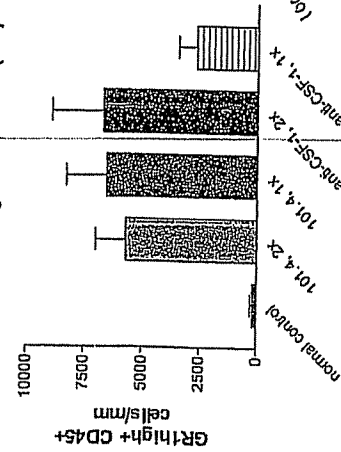
TITLE: anti-CSF-1 (3)

PAGE No. 63
DATE
PROJECT NO
NOTEBOOK NO 10015850

CD3+ CD45+ cells/mm in LP
population from colons of mice
on day 8, after DSS (1%)



GR1high+ CD45+ cells/mm in
LP population from colons of
mice on day 8 after DSS (1%)

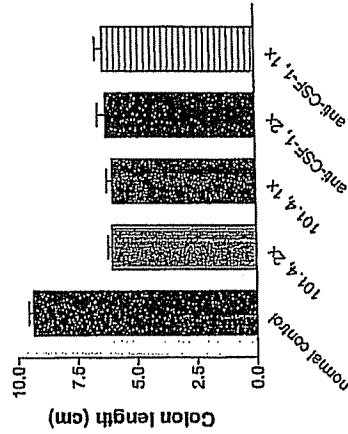


ASSESSED AND UNDERSTOOD
BY
DATE
INVENTED BY
RECORDED BY
DATE
DATE

TITLE: anti-CSF-1 (3)

PAGE No. 63
DATE
PROJECT NO
NOTEBOOK NO 10015850

Effect of anti-CSF-1 Ab on
colon length of mice after
addition of DSS (1%) in drinking
water for 7 days



(CSF-1)3jzmcData Table-2

	A		B		C		D		E	
	101.4, 2x		101.4, 1x		normal control-CSF-1, 2		normal control-CSF-1, 1			
1	5.70	5.30	5.30	5.30	5.30	5.30	5.30	5.30	5.30	5.30
2	5.40	5.60	5.60	5.60	5.60	5.60	5.60	5.60	5.60	5.60
3	6.50	6.50	6.50	6.50	6.50	6.50	6.50	6.50	6.50	6.50
4	7.00	5.20	5.20	5.20	5.20	5.20	5.20	5.20	5.20	5.20
5	5.70	5.70	5.70	5.70	5.70	5.70	5.70	5.70	5.70	5.70
6	5.80	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00
7	6.80	5.80	5.80	5.80	5.80	5.80	5.80	5.80	5.80	5.80
8	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00
9	6.10	6.70	6.70	6.70	6.70	6.70	6.70	6.70	6.70	6.70
10	5.20	7.00	7.00	7.00	7.00	7.00	7.00	7.00	7.00	7.00

10015850/63

ASSESSED AND UNDERSTOOD
BY
DATE
INVENTED BY
RECORDED BY
DATE
DATE

REDACTED

REDACTED

DATE _____
PROJECT NO _____
NOTEBOOK NO 10015850

TITLE: Anti-CSF-1 (3)

DATE _____
PROJECT NO _____
NOTEBOOK NO _____

REF: Anti-SF-1 (3)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100
101
102
103
104
105
106
107
108
109
110
111
112
113
114
115
116
117
118
119
120
121
122
123
124
125
126
127
128
129
130
131
132
133
134
135
136
137
138
139
140
141
142
143
144
145
146
147
148
149
150
151
152
153
154
155
156
157
158
159
160
161
162
163
164
165
166
167
168
169
170
171
172
173
174
175
176
177
178
179
180
181
182
183
184
185
186
187
188
189
190
191
192
193
194
195
196
197
198
199
200
201
202
203
204
205
206
207
208
209
210
211
212
213
214
215
216
217
218
219
220
221
222
223
224
225
226
227
228
229
230
231
232
233
234
235
236
237
238
239
240
241
242
243
244
245
246
247
248
249
250
251
252
253
254
255
256
257
258
259
260
261
262
263
264
265
266
267
268
269
270
271
272
273
274
275
276
277
278
279
280
281
282
283
284
285
286
287
288
289
290
291
292
293
294
295
296
297
298
299
300
301
302
303
304
305
306
307
308
309
310
311
312
313
314
315
316
317
318
319
320
321
322
323
324
325
326
327
328
329
330
331
332
333
334
335
336
337
338
339
340
341
342
343
344
345
346
347
348
349
350
351
352
353
354
355
356
357
358
359
360
361
362
363
364
365
366
367
368
369
370
371
372
373
374
375
376
377
378
379
380
381
382
383
384
385
386
387
388
389
390
391
392
393
394
395
396
397
398
399
400
401
402
403
404
405
406
407
408
409
410
411
412
413
414
415
416
417
418
419
420
421
422
423
424
425
426
427
428
429
430
431
432
433
434
435
436
437
438
439
440
441
442
443
444
445
446
447
448
449
450
451
452
453
454
455
456
457
458
459
460
461
462
463
464
465
466
467
468
469
470
471
472
473
474
475
476
477
478
479
480
481
482
483
484
485
486
487
488
489
490
491
492
493
494
495
496
497
498
499
500
501
502
503
504
505
506
507
508
509
510
511
512
513
514
515
516
517
518
519
520
521
522
523
524
525
526
527
528
529
530
531
532
533
534
535
536
537
538
539
540
541
542
543
544
545
546
547
548
549
550
551
552
553
554
555
556
557
558
559
560
561
562
563
564
565
566
567
568
569
570
571
572
573
574
575
576
577
578
579
580
581
582
583
584
585
586
587
588
589
590
591
592
593
594
595
596
597
598
599
600
601
602
603
604
605
606
607
608
609
610
611
612
613
614
615
616
617
618
619
620
621
622
623
624
625
626
627
628
629
630
631
632
633
634
635
636
637
638
639
640
641
642
643
644
645
646
647
648
649
650
651
652
653
654
655
656
657
658
659
660
661
662
663
664
665
666
667
668
669
670
671
672
673
674
675
676
677
678
679
680
681
682
683
684
685
686
687
688
689
690
691
692
693
694
695
696
697
698
699
700
701
702
703
704
705
706
707
708
709
710
711
712
713
714
715
716
717
718
719
720
721
722
723
724
725
726
727
728
729
730
731
732
733
734
735
736
737
738
739
740
741
742
743
744
745
746
747
748
749
750
751
752
753
754
755
756
757
758
759
760
761
762
763
764
765
766
767
768
769
770
771
772
773
774
775
776
777
778
779
780
781
782
783
784
785
786
787
788
789
790
791
792
793
794
795
796
797
798
799
800
801
802
803
804
805
806
807
808
809
810
811
812
813
814
815
816
817
818
819
820
821
822
823
824
825
826
827
828
829
830
831
832
833
834
835
836
837
838
839
840
84

PAGE No. 67

DATE
PROJECT NO
NOTEBOOK NO 1001585g.

ASSESSED AND UNDERSTOOD	DATE	INVENTED BY	DATE
by		RECORDED BY	DATE

ASSESSED AND UNDERSTOOD	DATE	INVENTED BY	DATE
BY		RECORDED BY	DATE

RETRACTED

REDACTED

09/05/2001
Mazda

49/05281001
Wang, C.

[illegible][illegible]